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EXAMINER
ZAGHMOUT, D

ART UNIT	PAPER NUMBER
1649	17

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/779,460

Applicant(s)
Goddijn et al.

Examiner
Ousama Zaghmout

Group Art Unit
1649



☒ Responsive to communication(s) filed on Nov 6, 1998

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1, 3-6, 8-12, 15-17, and 24-34 is/are pending in the application.

Of the above, claim(s) 16, 17, 24-29, and 32 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1, 3-6, 8-12, 15, 30, 31, 33, and 34 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 14

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED OFFICE ACTION

Response to amendment

The amendment filed 11-6-1998 (paper No.16) has been received and entered.

Claims 2, 7, 13, 14, and 18-23 have been canceled by the Applicants without prejudice.

Claims 1, 3-6, 8-12, 15-17, 24-34 are pending. Claims 3, 16-17 were restricted into a non-elected invention in the previous Office Action and were not examined on the merit in the previous Office Action. Of the newly added claims 25-34, only claims 30-31, 33-34 were examined on the merit; others 25-29, 32 were withdrawn from further consideration as they fall into a non-elected inventions. As such, only claims 1, 3-6, 8-12, 15, 30-31, 33-34 were considered on the merit in the instant Office Action. Claims 16-17, 24-29, 32 were withdrawn from further consideration. As claims 1, 4-5, 8-12, 15 are present in elected and non-elected inventions, these claims were examined to the extent that they read on the elected invention.

The IDS is noted.

Claim Rejections - 35 USC § 112

1st. Paragraph

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[Claims 1, 4-6, 8-12, 15 remain rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabled for the use of one trehalase inhibitor namely validamycin A, does not reasonably provide enablement for the use of other trehalase inhibitors. Applicants contend that those of skill in the art could routinely use the guidance provided by the specification to inhibit trehalase with other inhibitors. The Examiner respectfully disagrees. It is the specification not the skill of the art that should provide the enablement of the invention.] The claims are so broad that they encompass any trehalase inhibitor. The Examiner would like to draw the attention of the Applicants to the fact that enzyme inhibitors fall into two broad classes: those causing irreversible inactivation of enzymes and those whose inhibitory effects can be reversed. Inhibitors of the first class usually cause an inactivating, covalent modification of enzyme structure. The kinetic effect of irreversible inhibitors is to decrease the concentration of active enzyme, thus decreasing the maximum possible concentration of ES complex. Since the limiting enzyme reaction rate is often $k_2[ES]$, it is clear that under these circumstances the reduction of enzyme concentration will lead to decreased reaction rates. Note that when enzymes in cells are only partially inhibited by irreversible inhibitors, the remaining unmodified enzyme molecules are not distinguishable from those in untreated cells; in particular, they have the same turnover number and the same K_m . Turnover number, related to V_{max} , is defined as the maximum number of moles of substrate that can be converted to product per mole of catalytic site per second. As such, irreversible inhibitors are usually considered to be poisons and are generally unsuitable for practical purposes. In addition, the Examiner would like to bring to the attention of the

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here

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Applicants that reversible inhibitors can be divided into two main categories--- competitive inhibitors and noncompetitive inhibitors---with a third category, uncompetitive inhibitors, rarely encountered. Inhibitor Type: A. Competitive Inhibitor: specifically binds at the catalytic site, where it competes with substrate for binding in a dynamic equilibrium- like process. In a case like this, V_{max} is unchanged; K_m , as defined by $[S]$ required for $\frac{1}{2}$ maximal activity, is increased. B. Noncompetitive Inhibitor: the inhibitor binds E or ES complex other than at the catalytic site. Substrate binding unaltered, but ESI complex cannot form products. Inhibition cannot be reversed by substrate. In this case, K_m appears unaltered; V_{max} is decreased proportionately to inhibitor concentration. C. Uncompetitive Inhibitor: the inhibitor binds only to ES complexes at locations other than the catalytic site. Substrate binding modifies enzyme structure, making inhibitor- binding site available. Inhibition cannot be reversed by substrate. In this case, apparent V_{max} decreased; K_m , as defined by $[S]$ required for $\frac{1}{2}$ maximal activity, is decreased. As Applicants broadly claim any trehalase inhibitor, they fail to recognize that each inhibitor has a different biochemical criteria and mode of action as described above. This means that it is unpredictable how each one of these inhibitors will react upon contact with the enzyme and what the inhibition rate if any will take place. Furthermore, Applicants failed to address problems associated with all of the reversible inhibitors which is that when the inhibitor concentration drops, enzyme activity is regenerated. Usually these inhibitors bind to enzymes by non-covalent forces and the inhibitor maintains a reversible equilibrium with the enzyme. Taken together, Applicants failed to provide any description and enablement whatsoever for these

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claimed inhibitors of trehalase. Thus it is not readily predictable that the trehalose accumulation specifically disclosed will work with other inhibitors or other plants. Applicants have provided no specific guidance as to how to select inhibitors which will give the desired effect or provided guidance with regard to the technique to be used in the modification in these plants. One wishing to practice the invention is left to proceed through trial-and-error to see what will work and what will not. Based on this argument presented here and in the previous Office Action, the rejection of claims 1, 4-6, 8-12, 15 is maintained.

Rejections - 35 USC § 103

Claims 1, 4-6, 8-12, 15, 30-31, 33-34 are rejected under 35 U.S.C 103 (a) as being unpatentable over Kendall et al. (Phytochemistry. 1990. Vol. 29: 2525-2528) in view of Belknap et al. (American Potato Journal. 1994: Vol. 7: 285-296) for the reasons of record set forth at pages 10-12 of the Office action of 5-12-1998.

Applicants's arguments filed 11-6-1998 have been fully considered but they are not persuasive.

Applicants initially assert that the rejection of these claims should be withdrawn given that the teaching of Kendall et al which was cited by the Examiner do not render these claims obvious. The Applicants further argue that "it was not known whether validomycin A would have the same inhibiting effects in vivo as demonstrated in vitro experiments of Kendall et al. For

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example, it was not known, nor could it be derived from Kendall, et al, if validomycin would be able to enter the plant cells to exert its properties locally” [lines 1-4, page 8]. The Applicants further argue that one of skill in the art could not predict from any of the cited references with even reasonable expectation of success whether inhibiting the action of trehalase in vivo would result in an increase of trehalose content in plant cells [lines 5-7, page 8]. The Examiner respectfully disagrees. The Examiner would like to bring to the attention of the Applicants the fact that it is not necessary that a reference actually suggest changes or possible improvements which applicants made. In re Scheckler, 438 F.2d 999, 10001, 168 USBQ 716, 717 (CCPA 1971). It is assumed that every reference relies to some extent on the knowledge of persons skilled in the art to complement that which is disclosed therein. Further, the skilled artisan is presumed to know something more about the art than only what is disclosed in the applied references. In other words, the person having ordinary skill in the art has a level of knowledge apart from the content of the references. In re Bode, 550 F.2d 656,660,193 USPQ 12, 16, (CCPA 1977); In re Jacoby, 309 F. 2d 513, 516, 135 USPQ 317,319 (CCPA 1962). As such, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention. In this case, the inhibitor validomycin A is readily available in the teaching of Kendall et al. Furthermore, it was shown repeatedly to inhibit trehalase in cells growing in liquid. As such., a person with ordinary skill in the art would apply this inhibitor to any plant parts to allow trehalose accumulation realizing the importance of trehalose in mediating drought tolerance. As

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there was no accumulation of trehalose in cells growing in liquid by Kendall et al might be caused a number of factors such as the growing conditions of the cells, age of the cells, doubling time of the cells, the subculture time of the cells after adding the inhibitors, the number of cells growing and because of enzyme kinetics as mentioned above. It has nothing to do with ability of validamycin A to inhibit trehalase and/or causing the accumulation of trehalose. As such, even though this inhibitor did not cause accumulation of appreciable trehalose in cells, it does not mean by anyway that this inhibitor does not work on trehalose or if it is applied to plant parts will not work. It is not uncommon in the prior art to see inhibitor to work when applied in vitro and in vivo. Therefore, the arguments made by the Applicants that this inhibitor will not work at the plant level to accumulate trehalose is not persuasive. The Examiner further would like to bring to the attention of the Applicants that in considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom." In re Preda, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968) (A process for catalytically producing carbon disulfide by reacting sulfur vapor and methane in the presence of charcoal at a temperature of "about 750-830C" was found to be met by a reference which expressly taught the same process at 700C because the reference recognized the possibility of using temperatures greater than 750C. The reference disclosed that catalytic processes for converting methane with sulfur vapors into carbon disulfide at temperatures greater than 750C (albeit without charcoal) was known, and that 700C was "much lower than had previously proved feasible."); In re Lamberti, 545 F.2d 747, 750, 192

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USPQ 278, 280 (CCPA 1976) (Reference disclosure of a compound where the R-S-R¢ portion has "at least one methylene group attached to the sulfur atom" implies that the other R group attached to the sulfur atom can be other than methylene and therefore suggests asymmetric dialkyl moieties.). Furthermore, obviousness does not require absolute predictability, however, at least some degree of predictability is required. In the instant application, reasonable expectation of success is present as described above and in the previous Office Action. As such, these arguments by the Applicants were not persuasive.

The Applicants allege that the rejection made by the Examiner was based on impermissible hindsight which was born of reading the Applicants' disclosure (line 1-2, page 9). The Examiner respectfully disagrees. The Examiner would like to bring to the attention of the Applicants that "[a]ny judgement on obviousness is in a sense necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper." In re McLaughlin 443 F.2d 1392, 1395, 170 USPQ 209, 212 (CCPA 1971). As described above, the knowledge as described above and in the previous Office Action (pages 10-12) was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned and in the previous Office Action, there was no reason for hindsight from the present specification.

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For these reasons mentioned above, the combination of the references herein relied upon are deemed to establish a strong prima facie case of obviousness and thus the claims are deemed properly rejected. Therefore, the rejection for claims 1, 4-6, 8-12, 15, 30-31, 33-34 is maintained.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this **final action** is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Future Correspondence

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Ousama M-Faiz Zaghmout whose telephone number is (703) 308-9438. The Examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, L. Smith, can be reached on (703) 308-3909. The fax phone number for the group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to THE MATRIX CUSTOMER SERVICE CENTER whose telephone number is (703) 308-0196.

Ousama M- Faiz Zaghmout Ph.D

January 28, 1999


LYNETTE F. SMITH
PRIMARY EXAMINER
GROUP 1800